

Applicant: Robert J. Peach, et al.
U.S. Serial No: 09/865,321
Filed: May 23, 2001
Page: 2

In the Claims:

In compliance with the guidelines for making amendments, Applicants present all pending claims with status indicators.

Claims 67-96 are pending. Please add new claims 97-115 as follows:

--1-66. (CANCELLED)--

--67. (PREVIOUSLY PRESENTED) A soluble CTLA4 mutant molecule which binds CD80 and/or CD86 comprising an extracellular domain of CTLA4 as shown in SEQ ID NO. 8 beginning with alanine at position 26 or methionine at position 27 and ending with aspartic acid at position 150, or a portion thereof, wherein in the extracellular domain or portion thereof an alanine at position 55 is substituted with a tyrosine, and a leucine at position 130 is substituted with a glutamic acid.
--

--68. (PREVIOUSLY PRESENTED) A soluble CTLA4 mutant molecule comprising:
(a) an amino acid sequence beginning with methionine at position 27 and ending with aspartic acid at position 150 of SEQ ID NO.: 4, or
(b) an amino acid sequence beginning with alanine at position 26 and ending with aspartic acid at position 150 of SEQ ID NO.: 4. --

--69. (PREVIOUSLY PRESENTED) A soluble CTLA4 mutant molecule comprising:
(a) an amino acid sequence beginning with methionine at position 27 and ending with aspartic acid at position 150 of SEQ ID NO.: 4 or a portion thereof that binds CD80 and/or CD86, or
(b) an amino acid sequence beginning with alanine at position 26 and ending with aspartic acid at position 150 of SEQ ID NO.: 4 or a portion thereof that binds CD80 and/or CD86. --

Applicant: Robert J. Peach, et al.
U.S. Serial No: 09/865,321
Filed: May 23, 2001
Page: 3

- 70. (PREVIOUSLY PRESENTED) The soluble CTLA4 mutant molecule of claim 67, 68, or 69 further comprising an amino acid sequence which alters the solubility or affinity of the soluble CTLA4 mutant molecule. --
- 71. (PREVIOUSLY PRESENTED) The soluble CTLA4 mutant molecule of claim 70, wherein the amino acid sequence amino acid sequence which alters the solubility or affinity comprises an immunoglobulin. --
- 72. (PREVIOUSLY PRESENTED) The soluble CTLA4 mutant molecule of claim 71, wherein the immunoglobulin is an immunoglobulin constant region or portion thereof. --
- 73. (PREVIOUSLY PRESENTED) The soluble CTLA4 mutant molecule of claim 72, wherein the immunoglobulin constant region or portion thereof is mutated to reduce effector function. --
- 74. (PREVIOUSLY PRESENTED) The soluble CTLA4 mutant molecule of claim 72 or 73, wherein the immunoglobulin constant region comprises a hinge, CH2 and CH3 regions of an immunoglobulin molecule. --
- 75. (PREVIOUSLY PRESENTED) The soluble CTLA4 mutant molecule of claim 72, wherein the immunoglobulin constant region or portion thereof is a human or monkey immunoglobulin constant region. --
- 76. (PREVIOUSLY PRESENTED) A soluble CTLA4 mutant molecule comprising:
 - (a) an amino acid sequence beginning with methionine at position 27 and ending with lysine at position 383 of SEQ ID NO.: 4, or
 - (b) an amino acid sequence beginning with alanine at

Applicant: Robert J. Peach, et al.
U.S. Serial No: 09/865,321
Filed: May 23, 2001
Page: 4

position 26 and ending with lysine at position 383 of SEQ ID NO.: 4. --

- 77. (PREVIOUSLY PRESENTED) A soluble CTLA4 mutant molecule consisting of:
- (a) an amino acid sequence beginning with methionine at position 27 and ending with lysine at position 383 of SEQ ID NO.: 4, or
 - (b) an amino acid sequence beginning with alanine at position 26 and ending with lysine at position 383 of SEQ ID NO.: 4. --
- 78. (PREVIOUSLY PRESENTED) The soluble CTLA4 mutant molecule of claim 67, 68, 69, or 76 further comprising an amino acid sequence which permits secretion of the soluble CTLA4 mutant molecule. --
- 79. (PREVIOUSLY PRESENTED) The soluble CTLA4 mutant molecule of claim 78, wherein the amino acid sequence which permits secretion comprises an oncostatin M signal peptide. --
- 80. (PREVIOUSLY PRESENTED) A soluble CTLA4 mutant molecule comprising an amino acid sequence beginning with methionine at position 1 and ending with lysine at position 383 of SEQ ID NO.: 4. --
- 81. (PREVIOUSLY PRESENTED) A nucleic acid molecule encoding the soluble CTLA4 mutant molecule of claim 67, 68, 69, 76, 77 or 80. --
- 82. (PREVIOUSLY PRESENTED) The nucleic acid molecule of claim 81 comprising:
- (a) the nucleic acid molecule beginning with adenine at position 79 and ending with thymine at position 450 of SEQ ID NO:3, or

Applicant: Robert J. Peach, et al.
U.S. Serial No: 09/865,321
Filed: May 23, 2001
Page: 5

- (b) the nucleic acid molecule beginning with guanine at position 76 and ending with thymine at position 450 of SEQ ID NO:3. --
- 83. (PREVIOUSLY PRESENTED) The nucleic acid molecule of claim 81 comprising:
 - (a) the nucleic acid molecule beginning with adenine at position 79 and ending with adenine at position 1149 of SEQ ID NO.: 3 , or
 - (b) the nucleic acid molecule beginning with guanine at position 76 and ending with adenine at position 1149 of SEQ ID NO.: 3. --
- 84. (PREVIOUSLY PRESENTED) The nucleic acid molecule of claim 81 comprising the nucleic acid molecule beginning with adenine at position 1 and ending with adenine at position 1149 of SEQ ID NO.: 3. --
- 85. (PREVIOUSLY PRESENTED) A DNA molecule encoding a soluble CTLA4 mutant molecule, wherein the DNA molecule is deposited as ATCC No. PTA-2104. --
- 86. (PREVIOUSLY PRESENTED) A soluble CTLA4 mutant molecule encoded by the nucleic acid molecule designated ATCC No. PTA-2104. --
- 87. (PREVIOUSLY PRESENTED) A vector comprising the nucleic acid molecule of claim 81. --
- 88. (PREVIOUSLY PRESENTED) A vector comprising the DNA molecule of claim 85. --
- 89. (PREVIOUSLY PRESENTED) A vector encoding a soluble CTLA4 mutant molecule and deposited with the ATCC as ATCC No. PTA-2104. --

Applicant: Robert J. Peach, et al.
U.S. Serial No: 09/865,321
Filed: May 23, 2001
Page: 6

- 90. (PREVIOUSLY PRESENTED) A host cell having the vector of claim 87, 88, or 89. --
- 91. (PREVIOUSLY PRESENTED) The host cell of claim 90 which is a bacterial or eukaryotic cell. --
- 92. (PREVIOUSLY PRESENTED) The host cell of claim 91, wherein the eukaryotic cell is a COS cell or a Chinese Hamster Ovary (CHO) cell. --
- 93. (PREVIOUSLY PRESENTED) A method for producing a soluble CTLA4 mutant molecule comprising growing the host cell of claim 90 so as to produce the soluble CTLA4 mutant molecule in the host cell, and recovering the molecule so produced. --
- 94. (PREVIOUSLY PRESENTED) A soluble CTLA4 mutant protein produced by the method of claim 93. --
- 95. (PREVIOUSLY PRESENTED) A soluble CTLA4 mutant molecule comprising the entire extracellular domain of the soluble CTLA4 mutant molecule encoded by the nucleic acid molecule designated ATCC No. PTA-2104. --
- 96. (PREVIOUSLY PRESENTED) A pharmaceutical composition comprising a soluble CTLA4 mutant molecule of claim 67, 68, 69, 76, 77, 94, or 95 and a pharmaceutically acceptable carrier. --
- 97. (NEW) A CTLA4 mutant molecule comprising an amino acid sequence which begins with methionine at position +1 and ends with aspartic acid at position +124

Applicant: Robert J. Peach, et al.
U.S. Serial No: 09/865,321
Filed: May 23, 2001
Page: 7

as shown in Figure 7, or which begins with alanine at position -1 and ends with aspartic acid at position +124 as shown in Figure 7. --

- 98. (NEW) The CTLA4 mutant molecule of claim 97, further comprising an amino acid sequence which alters the solubility, affinity or valency of the CTLA4 mutant molecule. --
- 99. (NEW) The CTLA4 mutant molecule of claim 98, wherein the amino acid sequence which alters the solubility or affinity comprises an immunoglobulin moiety. --
- 100. (NEW) The CTLA4 mutant molecule of claim 99, wherein the immunoglobulin moiety is an immunoglobulin constant region or portion thereof. --
- 101. (NEW) The CTLA4 mutant molecule of claim 100, wherein the immunoglobulin constant region comprises a hinge, CH2 and CH3 regions of an immunoglobulin molecule. --
- 102. (NEW) The CTLA4 mutant molecule of claim 100, wherein the immunoglobulin constant region or portion thereof is a human or monkey immunoglobulin constant region. --
- 103. (NEW) The CTLA4 mutant molecule of claims 99, wherein the immunoglobulin moiety comprises one or more mutations to reduce effector function. --
- 104. (NEW) The CTLA4 mutant molecule of claims 99, wherein the immunoglobulin moiety comprises a hinge and any or all of the cysteine residues within the hinge are substituted with serine. --

Applicant: Robert J. Peach, et al.
U.S. Serial No: 09/865,321
Filed: May 23, 2001
Page: 8

- 105. (NEW) The CTLA4 mutant molecule of claim 104, wherein a cysteines at position +130 is substituted with a serine, a cysteine at position +136 is substituted with a serine, and a cysteine at position +139 is substituted with a serine, as shown in Figure 7. --
- 106. (NEW) The CTLA4 mutant molecule of claim 100, wherein the immunoglobulin constant region is mutated to include a cysteine at position +130 substituted with a serine, a cysteine at position +136 substituted with a serine, a cysteine at position +139 substituted with a serine, and a proline at position +148 substituted with serine, as shown in Figure 7. --
- 107. (NEW) The CTLA4 mutant molecule of claim 99, wherein the immunoglobulin moiety comprises an amino acid sequence which begins with glutamic acid at position +126 and ends with lysine at position +357, as shown in Figure 7. --
- 108. (NEW) The CTLA4 mutant molecule of claim 97, further comprising a junction amino acid residue which is located between the amino acid sequence which ends with aspartic acid at position +124 and the immunoglobulin moiety. --
- 109. (NEW) The CTLA4 mutant molecule of claim 108, wherein the junction amino acid residue is glutamine. --
- 110. (NEW) The CTLA4 mutant molecule of claim 97, comprising an amino acid sequence which begins with methionine at position +1 and ends with lysine at position +357 as shown in Figure 7, or which begins with alanine at position -1 and ends with lysine at position +357 as shown in Figure 7. --
- 111. (NEW) The CTLA4 mutant molecule of claims 97, further comprising an amino acid sequence which permits secretion of the soluble CTLA4 mutant molecule. --

Applicant: Robert J. Peach, et al.
U.S. Serial No: 09/865,321
Filed: May 23, 2001
Page: 9

- 112. (NEW) The CTLA4 mutant molecule of claim 111, wherein the amino acid sequence comprises an oncostatin M signal peptide. --
- 113. (NEW) The CTLA4 mutant molecule of claims 97, that has a slower dissociation rate from binding CD86 than wild type CTLA4. --
- 114. (NEW) The CTLA4 mutant molecule of claims 97, that is soluble. --
- 115. (NEW) The CTLA4 mutant molecule of claim 97, that is encoded by the nucleic acid molecule deposited as ATCC No. PTA-2104. --